REMARKS

Favorable reconsideration is respectfully requested.

The claims are 1 to 12.

The above amendment renders moot the rejection of claims 13 and 14 under 35 U.S.C. 101 and 112.

Claims 1 to 14 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Yanagawa (EP 0 681 833 A2) in view of Staniforth et al (US 5,948,438).

This rejection is respectfully traversed.

As is recognized by the Official Action, the "porous, spherical calcium carbonate" which is used in the present invention is mentioned neither in Yanagawa nor in Staniforth et al. ✓

Said calcium carbonate has a specific internal structure. In more detail, it comprises trabeculate or needle-shaped crystals or an aggregation of the parallel intergrowth of these forms. Furthermore, owing to its particle diameter (see claims 1, 2 and 4 and Figure 1 as well), said calcium carbonate, when used as a carrier, is capable of significantly raising serum insulin concentration up to about 6.8 times as high as achieved by a particle diameter-unregulated calcium carbonate pharmacopeial product which was or is being normally employed in the art, or up to about 1.8 times even in comparison with calcium carbonate whose particle diameter has been regulated within 20 to 32 μm (see C_{max} values in Table 2 and Figure 2).

The present invention, which produces such remarkable actions and effects, has been completed only by the finding which is mentioned in the present specification, page 2, lines 17 to 22, i.e., as follows:

"...the present inventor investigated the effect of combinations of insulin and various carriers on the nasal absorption of insulin and thereby the use of a specific calcium carbonate structure for intranasal insulin delivery was found to significantly increase blood insulin levels and significantly decrease blood-sugar levels."

Turning to the cited references:

Yanagawa (a counterpart of JP A 8 27031 which is mentioned in the present specification, page 1, line 25) discloses using, as a carrier for nasally administrable composition, a wide variety

of physiologically acceptable powdery or crystalline polyvalent metal compound carriers. In this reference, the use of calcium carbonate is also mentioned.

Yanagawa, however, only shows that calcium carbonate is an example to be selected from among various carriers, and thus has no such teaching as to give incentive for skilled persons to choose calcium carbonate whose structure, in particular internal structure, has been changed.

Of course, no art-skilled person could have foreseen from Yanagawa that calcium carbonate having such a specific structure as in the present invention would produce remarkable actions and effects.

Staniforth et al., on the other hand, has a passage to the following effect as the Official Action notes:

"pharmaceutical formulations having improved disintegration and/or absorptivity wherein calcium carbonate is used in combination with porous particles of microcrystalline cellulose" (emphasis added) (see column 4, lines 6 to 8, with regard to the prior art)

The problem which Staniforth et al. try to resolve is, however, as mentioned in column 4, lines 35 to 38, i.e., as follows:

"There still remains a need in the industry for a pharmaceutical excipient which possesses excellent compressibility whether utilized in a direct compression or wet granulation procedure."

In order to satisfy the above-mentioned need, Staniforth et al. use "the novel agglomerated microcrystalline cellulose excipient" (see column 6, lines 58 to 59).

Staniforth et al. further refer to combined use of said agglomerated microcrystalline cellulose excipient with "augmenting agents" (e.g., silicon dioxide). Staniforth et al. state that, if desired, filler can be included in the final product, and mention "calcium carbonate" as an example of filler (see column 17, lines 53 to 63, in particular line 61).

Staniforth et al. thus teach that it is advantageous to choose specific ones from among various kinds of microcrystalline cellulose, with a view to providing, in particular, oral solid dosage form. Staniforth et al., however, give no incentive to choose such a specific calcium carbonate as in the present invention.

As mentioned above, Staniforth et al. simply teach that "calcium carbonate" can be used as filler if desired. It could be said that such a statement would have made it rather difficult for skilled persons to conceive of the idea of the present invention.

For the foregoing reasons, it is apparent that the present invention is unobvious from a combination of Yanagawa and Staniforth et al..

No further issues remaining, allowance of this application is respectfully requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned at the telephone number below.

Respectfully submitted,

Ryoichi NAGATA

By: _____

Matthew Jacob
Registration No. 25,154
Attorney for Applicant

MJ/jef
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
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